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REMARKS

Claims 1-5, 7-15, 17, 37-42 are pending herein, claim 38 having been deleted without prejudice herein.

No new issues are raised by the above claim amendments (see claim 2, claim 4 and previously pending claim 38).

The Office Action indicates that claims 4, 5 and 9 are withdrawn from consideration as directed to non-elected species. Claim 9, however, claims polystyrene *microparticles* (as opposed to a polymer incompatible component) and thus is not directed to a non-elected species as asserted in the present Office Action. Claims 4 and 5 have not been deleted at this time because, as indicated in the Office Action mailed July 16, 2002, the restriction requirement between the linked inventions is subject to the non-allowance of the linking claim (e.g., claim 1).

Responsive to the Office Action mailed April 11, 2003 in the above matter, please consider the following remarks.

A. Objection of Claims 1 and 7-17.

Claims 1 and 7-17 are objected to in the Office Action of April 11, 2003, as purportedly embracing non-elected Group III claims readable on the limitation of exposing the claimed suspension to an *incompatible condition*.

Claim 1 explicitly specifies that the suspension is contacted with an *incompatible component* comprising a metal or a polymer (as opposed to an incompatible condition). Claims 7-15 and 17 depend from claim 1 (claim 16 is canceled) and therefore further limit claim 1. Accordingly, reconsideration and withdrawal of the objection to claims 1 and 7-17 are respectfully requested.

B. Rejection of Claims under 35 U.S.C. 112, first paragraph–Written Description.

Claims 1, 7-8, 10-15, 17 and 37 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was allegedly not described in the specification in such as way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time that the application was filed, had possession of the claimed invention. In

particular, the Office Action contents that the claims were directed to any incompatible component of a pharmaceutical article, while the specification only teaches and discloses medical delivery devices containing metals and polymers as incompatible components.

Although Applicants do not agree with the Office Action, to advance prosecution in the present application, claim 1 (the only independent claim pending in the present application) has been amended such that it presently claims an incompatible component comprising a metal or a polymer, which is a component of a drug delivery medical device.

It is therefore believed that the outstanding rejection of claims 1 and 7-17 under written description requirement of 35 U.S.C. 112, first paragraph, has been rendered moot by the above amendment. Reconsideration and withdrawal of this rejection are therefore requested.

C. Rejection of Claims under 35 U.S.C. 112, first paragraph--Enablement.

Claims 1, 7-8, 10-15, 17 and 37 are presently rejected as allegedly not being enabled under 35 U.S.C. 112, first paragraph.

As above, Applicants do not agree with the Office Action. However, to advance prosecution in the present application, claim 1 has been amended to reflect the text of pages 4 and 5 of the Office Action, wherein an indication is given regarding the claim scope to which Applicants are entitled under the enablement provisions of under 35 U.S.C. 112, first paragraph. In particular, claim 1 has been amended such that it presently claims an incompatible component comprising a metal or a polymer, which is a component of a drug delivery medical device,

It is therefore believed that the outstanding rejection of claims 1, 7-8, 10-15, 17 and 37 under the enablement provisions of 35 U.S.C. 112, first paragraph, is now moot. Reconsideration and withdrawal of this rejection are therefore requested.

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D. Rejection of Claims 1-3, 7-8, 10-17 and 37-42 under 35 U.S.C. 102(e)--Pinchuk

Claims 1-3, 7-8, 10-17 and 37-42 are presently rejected under 35 U.S.C. 102(e) as being anticipated by Pinchuk et al., U.S. Pat. Appln. Pub. No.2002/0107330 ("Pinchuk"). Applicants respectfully traverse this rejection and its supporting remarks.

Specifically, the Office Action states, *inter alia*, the "[t]he teaching of a suspension comprising the block copolymers and a therapeutic agent, wherein the copolymer and therapeutic agents are both present or commingled in a buffered solution before being exposed to a medical device, is clearly taught on page 9, paragraph 0190, and paragraph 0196."

Applicants disagree. Paragraph 0190 actually reads as follows (emphasis added):

> If desired, the copolymer/solvent mixture can contain more than one *solvent* (for example, one *solvent appropriate for the block copolymer* and a different solvent appropriate for the therapeutic agent). As a specific non-limiting example, where paclitaxel is selected as a drug and where the copolymer is the triblock polystyrene-polyisobutylene-polystyrene, a *solution* made from toluene, tetrahydrofuran, paclitaxel and the copolymer can be used.

Hence, this paragraph is directed to an *organic solution* that is used to form a medical device or a portion of the same (see paragraph 0189), rather than a *suspension*, and clearly not a suspension wherein copolymers and therapeutic agents are "commingled in a buffered solution" as asserted in the Office Action.

In this regard, it is noted that claim 1 is directed, *inter alia*, to a pharmaceutically acceptable suspension in which polymer microparticles are commingled with a pharmaceutically active agent. The compositions of paragraph 190, on the other hand, are polymer *solutions* (i.e., liquids), as opposed to the *suspensions* (i.e., compositions comprising a dispersed solid phase within a liquid phase) claimed in claim 1.

Nor are the compositions of paragraph 190 of Pinchuk pharmaceutically acceptable, because the tetrahydrofuran and toluene solvents, which are toxic, are present in substantial quantities. (See, for example, the drying process described in Example 4 of Pinchuk, which is employed to remove residual solvents.)

Paragraph 0196 (to follow, emphasis added) is non-anticipatory for reasons akin to those discussed above in connection with paragraph 190:

> If desired, a therapeutic agent of interest can be provided at the same time as the copolymer coating, for example, by adding it to a *copolymer melt* during thermoplastic processing or by adding it to a *copolymer solution* during solvent-based processing as discussed above. Alternatively, it can be added after the coating is formed as discussed further below.

The same is true for Example 2, which was cited in the Office Action.

The Office Action further asserts that "the microparticles are provided in an amount of an exemplified 1 wt%." However, it is respectfully submitted that none of the citations which are offered in support of this assertion appear to be concerned with microparticles.

The Office Action also refers to dimensions of 0.5 to 50 microns in paragraph 195. However, these dimensions are coating thicknesses. Note from paragraph 0033 of the present specification that "microparticles" are small particles ranging in largest dimension from 0.01 to 1000 microns, and that they can be of any shape, including spherical, rod-shaped particles, irregularly shaped, etc. Hence, it is not seen what connection exists between a coating on a medical device, as described in paragraph 195 of Pinchuk, and a microparticle-containing suspension as presently claimed in claim 1.

For at least the above reasons, it is respectfully submitted that claim 1 is *not* anticipated by Pinchuk. Hence, claims 2, 3, 7-8, 10-17 and 37-42, which depend from claim 1, are not anticipated by Pinchuk for at least the same reasons.

Accordingly, reconsideration and withdrawal of the rejection of claims 1-3, 7-8, 10-17 and 37-42 as being anticipated by Pinchuk are respectfully requested.

E. Rejection of Claims 1, 2, 7, 9-15, 17, 37-42 under 35 U.S.C. 102(e)--Mathiowitz

Claims 1, 2, 7, 9-15, 17 and 37-42 are presently rejected under 35 U.S.C. 102(e) as being anticipated by Mathiowitz et al., U.S. Pat. No. 6,248,720 B1 ("Mathiowitz"). Applicants respectfully traverse this rejection and its supporting remarks.

Specifically, Mathiowitz is directed to microparticles, within which nucleic acids are *encapsulated*. See, e.g., col. 1, lines 49-53 and lines 57-59, col. 4, lines 55-58, Examples 1-4, etc. In contrast to Mathiowitz, the pharmaceutically active agent of claim 1 of the present application is *not encapsulated* within the microparticles. Rather, the pharmaceutically active agent and polymer microparticles in claim 1 are *commingled*

within the suspension. See, for example, paragraph [0044] of the present specification. See also Example 1, in which an aqueous adenoviral solution and an aqueous suspension of polystyrene beads are commingled to form a pharmaceutically acceptable suspension.

In other words, the pharmaceutically active agent of Mathiowitz is on the *inside* of the microparticles. In contrast, in the presently claimed invention, the pharmaceutically active agent is commingled with, and therefore *outside* of the microparticles.

Moreover, Mathiowitz does not teach or suggest contacting a pharmaceutically acceptable suspension with an incompatible metal or polymer component of a drug delivery medical device as presently claimed, such that the presence of the polymer microparticles results in a pharmaceutical effectiveness of the pharmaceutically active agent, which is greater than the pharmaceutical effectiveness of the pharmaceutically active agent when contacted with the incompatible component in the absence of the polymer microparticles.

In this connection, note that the metal compounds referred to at col. 13, lines 21-45 of Mathiowitz (which are not medical device components) actually enhance the pharmaceutical effectiveness of the polymer.

For at least the above reasons, it is respectfully submitted that claim 1 is not anticipated by Mathiowitz. Claims 2, 7, 9-15, 17 and 37-42, which depend from claim 1, are patentable over Mathiowitz for at least the same reasons.

Accordingly, reconsideration and withdrawal of the rejection of claims 1, 2, 7, 9-15, 17 and 37-42 as being anticipated by Mathiowitz are respectfully requested.

F. Rejection of Claims 1-3, 7-8, 10-15, 17 and 37-42 under 35 U.S.C. 103(a)

Claims 1-3, 7-8, 10-15, 17 and 37-42 are presently rejected under 35 U.S.C. 103(a) as being obvious over Mathiowitz taken with WO 01/30403 ("Barry") or Pinchuk.

In essence, the Office Action cites Barry and Pinchuk for disclosing the existence of metallic and/or polymeric catheters for the delivery of biologically active agents to cells *in vivo*. Applicants respectfully traverse this rejection and its supporting remarks.

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Specifically, the presently pending claims are patentable over Mathiowitz and Pinchuk for the reasons set forth above. Moreover, the disclosure cited in Barry does not make up for the above noted deficiencies in Mathiowitz (or Pinchuk).

For at least these reasons, it is respectfully submitted that claims 1-3, 7-8, 10-15, 17 and 37-42 are patentable under 35 U.S.C. 103(a) over Mathiowitz in view of Barry or Pinchuk.

CONCLUSION

Applicants submit that this application is in condition for allowance, early notification of which is earnestly solicited. The Examiner is encouraged to contact the undersigned at (703) 433-0510 to discuss any outstanding issues in this case.

FEES

The Office is authorized to charge any fees required in connection with this application to deposit account number 50-1047.

Respectfully submitted,

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I hereby certify that this correspondence is being sent to the United States Patent and Trademark office via Facsimile to: 703-872-9307 on June 11, 2003.

David B. Bonham
(Printed Name of Person Mailing Correspondence)

(Signature)